HEMANGIOMAS OF CEREBELLUM AND RETINA (LINDAU'S DISEASE)

WITH THE REPORT OF A CASE*

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Angiomas of the retina have long been recognized by ophthalmologists under the name of v. Hippel's disease; cysts of the cerebellum have come to be frequently operated upon by neuro-surgeons, and some of them prove to have an angiomatous nodule in their walls; cystic kidneys and cysts of the pancreas that have given no symptoms during life are occasionally found postmortem by pathologists. That these and other lesions not uncommonly occur together in the same patient and constitute a disorder with hereditary tendencies has recently (1926)[27] been clearly shown by Arvid Lindau, of Lund, which fact well justifies the eponym used in the title of this paper.

From a primary interest in the pathologic nature of the cerebellar cysts, two examples with a hemangiomatous basis having come to his attention, Lindau was led to seek for similar specimens in the various pathologic collections in Sweden and on the Continent, with the result that 15 unreported examples were assembled. In examining the postmortem protocols of these cases, he was struck by the frequency with which the cerebellar cyst was associated with angiomatous and cystic lesions in other parts of the body.

One of the specimens, discovered in Stockholm (Lindau's

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Case 4), had been secured in 1922 from an autopsy, the records of which showed that, in addition to the angiomatous cyst of the cerebellum, there had been found a bilateral adenoma of the suprarenal glands. The patient, moreover, had been known clinically to have had what was diagnosed as "an arteriovenous aneurysm" of the right retina, for which the eye had been enucleated eight years previously, the specimen having been preserved without histologic examination. When cut and examined microscopically, a small capillary hemangioma of the peripheral retina was brought to view.

Because of this interesting disclosure, Lindau was drawn into a study of angiomatosis retinæ, a rare malady with a familial tendency, and of which some 50 cases have been reported. In reviewing these cases, he found that approximately 20 per cent. of the patients had been known to have intracranial complications, accounting for the tradition among ophthalmologists that v. Hippel's disease was a serious malady. In two of the cases, indeed (those of Czermak[9] and Seidel[35]), a postmortem examination had served to show that death had been due to the effects of a coincidental cerebellar cyst.

Though previous observers, therefore, had noticed this combination of retinal and cerebellar lesions, there was no reason to suppose that they were correlated until Lindau's studies brought to light the fact that additional changes in other organs were likely to be found: namely, cysts of the kidney and of the pancreas, hypernephromas, and occasionally multiple angioblastic tumors of the spinal cord. Evidently, therefore, here was a new and previously unrecognized disease.

Lindau succeeded in gathering from the literature and from unpublished pathologic records 15 examples of this disorder, which he designated "angiomatosis of the nervous system." A year later, in a second paper,[28] written particularly to draw the attention of ophthalmologists to the subject, he an-

nounced that in the interim four additional examples had been disclosed at postmortem examinations. One of these cases had been personally observed; information concerning the others had been supplied by Hammar,[19] of Amsterdam, by Rochat and Tresling, of Groningen, and by Wohlwill, of Hamburg. The history of Lindau's personally observed case is briefly as follows:

The patient, whose brother had previously died from a presumed cerebellar tumor, succumbed to an operation undertaken for comparable symptoms, and at autopsy there was found a *cystic hemangioma of the cerebellum, cystic pancreas, cysts of the kidney, hypernephromas of kidney, and similar appearing tumors of the epididymis.* A histologic examination of the eye, in which nothing more than a choked disc had clinically been recognized, revealed a *hemangioma of the retina* of microscopic size.

The cases of Rochat[33] and of Wohlwill[37] have since (1927) been published, and still another example, the twentieth, has been recorded by Shuback,[36] a cystic hemangioma of the cerebellum having been found in association with a cystic pancreas and cystic kidneys in which there were two small hypernephromas.

To these 20 cases we are able to add one more, it being the first one, so far as we are aware, in which the histologic diagnosis of the cerebellar lesion has been verified during the life of the patient.

On December 8, 1922, Frank McA., a truck driver, thirty years of age, entered the Peter Bent Brigham Hospital with the chief complaint of suboccipital headaches which had begun without apparent cause about two months previously.

There was nothing notable in his past history apart from the fact that he was supposed to have had an attack of cerebrospinal meningitis in 1919.

In spite of some peculiarities of the clinical picture, notably astereognosis of the left hand and only a questionable papilledema, he showed a sufficiently definite cerebellar syndrome (nystagmus, positive Romberg, unsteadiness of gait, etc.) to justify the diagnosis of a cerebellar tumor.

On December 13th, in the course of the usual bilateral cerebellar exploration, a low-lying and superficially placed cyst was exposed (Fig. 1). The cyst contained xanthochromic fluid, and on opening it a small mural nodule of tumor was found laterally placed about at the level of the foramen magnum, in which it had become

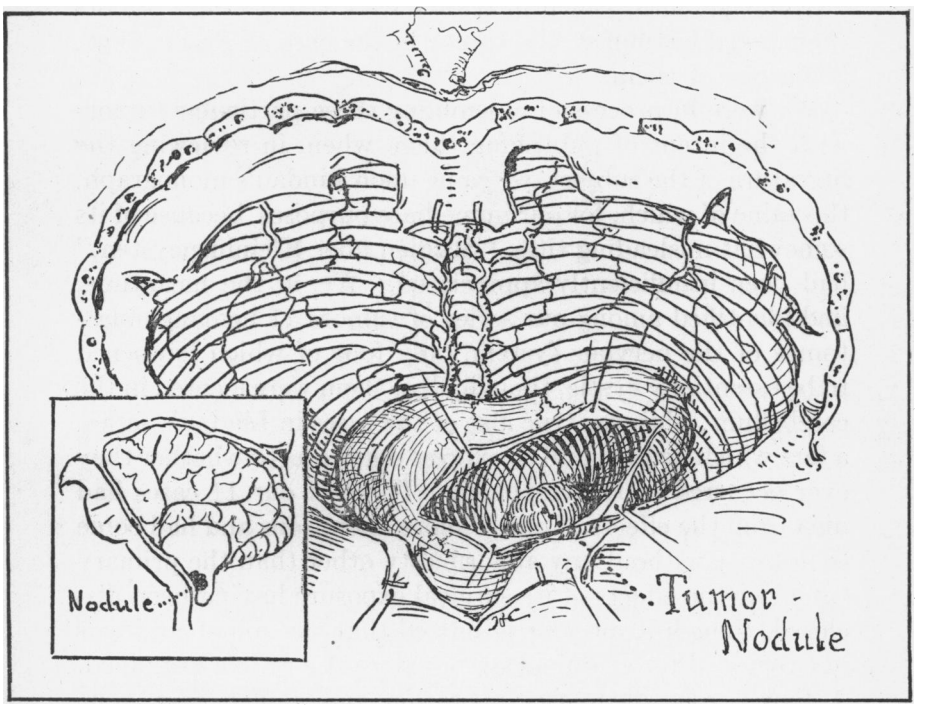


Fig. 1.—Immediate postoperative sketch giving general appearance of operative field with cyst and position of nodule.

engaged. Though the tumor nodule was quite vascular, it was successfully excised.

The patient made an uneventful recovery and was discharged on January 3d practically free from symptoms.

The lesion was supposed to be a gliomatous cyst and the tissue was submitted to the pathologic laboratory as a vascular gliomatous nodule, a gross diagnosis which received histologic confirmation.

It was at about this time (1922) that we had begun to attempt a classification[1] of the gliomas on a clinico-pathologic basis. In the course of this study we soon found that there were a number of tumors in the series that, in the past, for want of proper differential stains, had been regarded as vascular gliomas, which in reality were blood-vessel tumors (hemangioblastomas), the tumor in the case of Frank McA. being one of them.

We were in process of assembling these particular tumors with the intent of publishing them, when, in reviewing the literature of the subject, we came upon Lindau's monograph, the value of which, for our immediate purposes, because of its somewhat misleading title, "Studien über Kleinhirncysten," had been insufficiently appreciated. We, in the meantime, had identified among our series of tumors 11 hemangioblastomas of the nervous system, only four of which happened to be essentially cystic, though all of them were located in the cerebellum; this was true also of the cases in Lindau's series, a fact which had led him to express doubts as to whether they ever occurred in the cerebrum. Three of our 11 cases had died from the effects of one or more operations and had come to autopsy without any abnormality other than the primary tumor or the effects of its surgical exposure having been disclosed, though it must be admitted that the spinal cord was not removed for examination nor were the retinæ examined. A fourth case died after operation and a fifth case some months afterward at home, neither of them with postmortem examinations.

Though these five cases were beyond recall, we promptly set about to have the eyegrounds of the six surviving cases reëxamined on the assumption that in our own examination of the fundus, restricted largely to the papilla for evidences either of choked disc or of optic atrophy, which rarely necessitates dilatation of the pupil, we had probably overlooked or

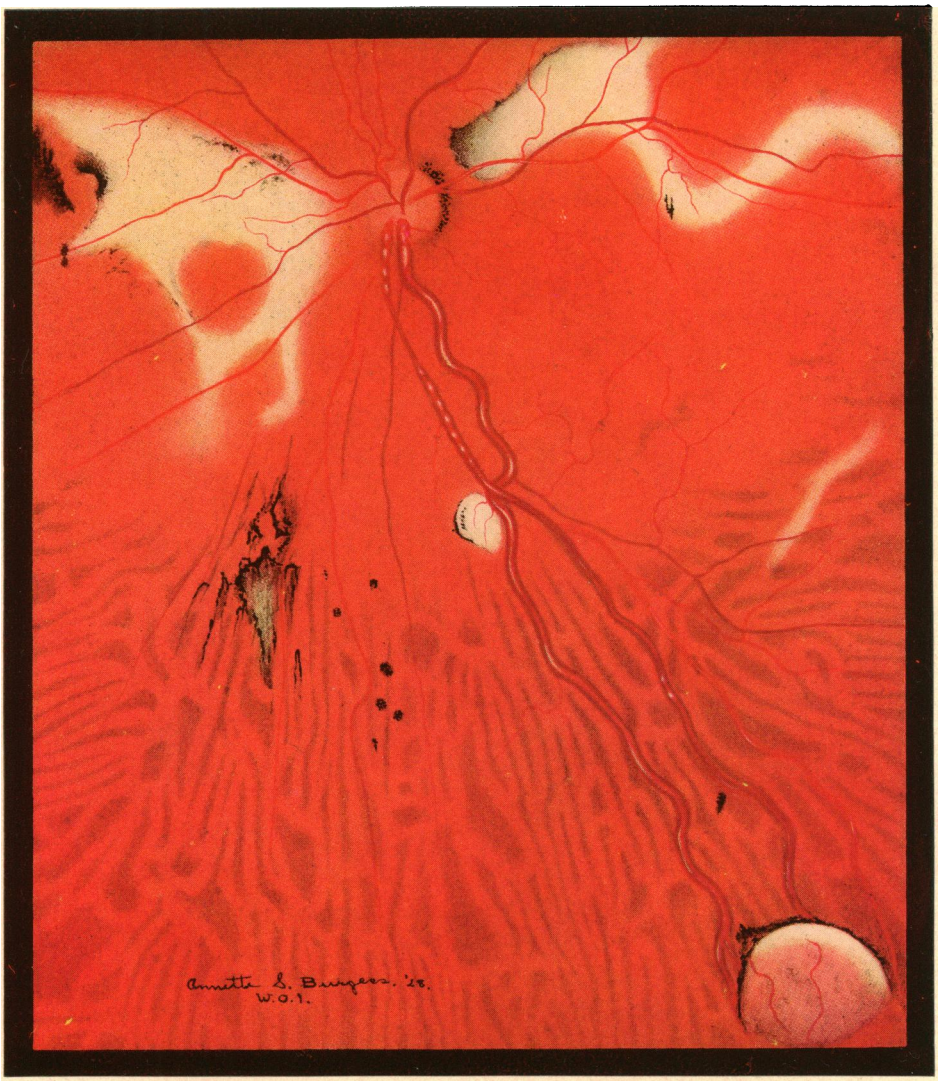


Fig. 2.—Drawing of the patient's eyeground. (Kindness of Dr. William H. Wilmer.)

failed to recognize an outlying angioma of the peripheral retina.*

As chance would have it, Frank McA., whose clinical history has been briefly given, was the first to report and proved to be the only one of the six to show an unmistakable retinal angioma (Fig. 2). We are aware, of course, from Lindau's second paper, that the lesion may be a microscopic one and early in its course may, therefore, not be discernible by ophthalmoscopic examination, but the positive finding in even this one of our patients has so interested us that we have felt impelled to give an account of the case, independent of our study of the blood-vessel tumors in general.

After the detection of the retinal lesion in this patient a detailed review by Dr. J. F. Fulton of his family and personal history has brought out additional facts, secured from an older sister as chief informant, which may now be given:

Family history of "eye trouble" (first generation). The patient's father, who died at thirty-six years of age, had always had poor eyesight and wore "thick spectacles." For four or five years before his death he was largely confined to bed because of gastric symptoms, dizziness, and inability to walk. There was disagreement as to whether he had stomach or brain trouble. He died suddenly in an attack of some kind, and after an examination the attending doctor stated that death had been caused by rupture of a cystic tumor of the brain called a sarcoma.

An aunt is said to have died under very similar circumstances, also from "a ruptured cystic sarcoma," eight years previously, and it is recalled by members of the family that the doctor had commented upon the fact that it was peculiar both brother and sister should have died from such an unusual disorder.

Of the *second* (the patient's) *generation*, there are two sisters and one brother surviving. The older sister (the principal informant) is forty-five years of age. She states that the family inherit poor eyesight and all tend to have rather prominent eyes. She herself

* We wish to express our obligations to Dr. W. H. Wilmer of Baltimore, to Drs. E. T. Smith and A. L. Prince, of Hartford, to Drs. H. H. Glosser and Park Lewis, of Buffalo, and to Dr. George S. Derby, of Boston, who have kindly examined these patients for us.

has had poor vision, particularly in the left eye, since childhood. She shows a high hypermetropic refractive error, the fundus being best seen on the right with a +5 and on the left with a +7 lens. She is given to recurrent suboccipital headaches, but the eye-grounds show no proliferative retinitis or evidence of an angioma.

The patient himself, when eight years of age, because of poor vision, was examined by Dr. Allen Greenwood, who noted (1897) the high refractive error and prescribed glasses, but informs us that he made no notes of a fundus examination.

The second sister is now thirty years of age, and was born with "ruptured tear-ducts," but is said to have no particular trouble with her eyesight. (She has not been examined.) A brother died in infancy of unknown cause.

Third Generation: The patient has been married twenty-one years and there are eight healthy children. The oldest child, a daughter, aged twenty, is married and has one offspring apparently with normal fundi. The second daughter, aged nineteen, has had eye trouble since childhood, with recurrent suboccipital headaches. The eight children (six girls and two younger boys, aged seven and nine) have all been examined, and though two of them show marked hypermetropic error of refraction, no retinal abnormalities could be detected.

It may be too early for the lesion to manifest itself in these children, in which connection it should be noted that the cerebellar lesion in the 11 cases in our series and in those collected by Lindau did not show symptoms of its presence till the age of the patients averaged thirty-four years.

Past History: The patient's presumed attack of "cerebrospinal meningitis" has been carefully inquired into and doubts may be had of this diagnosis. It appears from the records of the hospital where he was confined that on October 7, 1919, while starting his auto truck, the crank "kicked," pressing his shoulder upward, causing pain and stiffness of the neck; that his symptoms, chiefly of suboccipital headache severe enough to require repeated doses of morphin, had come on abruptly. He showed retraction of the neck, a positive Kernig sign, and a lumbar puncture gave a bloody fluid in which a house officer is said to have found "intra- and extracellular diplococci." He was confined to the hospital for five weeks.

His attendant of the time admits that the clinical record is not very clear and it seems far more probable to us that the sudden symptoms were due to a traumatic rupture of the thin-walled cyst

caught in the foraminal ring. From the time of this attack in 1919 to 1922, when he first came under our care, he appears to have been comparatively free from discomforts, though in all probability a neurologic examination in the interval would have shown some residual cerebellar symptoms.

Ophthalmologic Notes.—At the time of the patient's first admission to the Peter Bent Brigham Hospital in 1922 there was a difference of opinion among several observers as to whether there was a choked disc. It was recognized that there was a congenital refractive error. Haziness of the disc margins was noted, and the presence of some new tissue formation, which was regarded as possibly a sequel of the supposed meningitis. One observer, while doubting the presence of tumor or pressure, noted, without mention of the eye involved, that there was an enormous vein which ran downward in a very tortuous course toward the lower retina. No particular significance was attached to this and none of the other five observers who gave notes from time to time on the condition of the eyegrounds made mention of the fact.

In 1924, a year or more after the patient's cerebellar operation, presumably owing to failure of vision, he was examined at the Massachusetts Eye and Ear Infirmary, where an ophthalmologic examination must have been made, for it was noted that the retinæ were not detached; but the angioma was not detected.

Thus, out of many examinations during the patient's life by at least eight observers, the presence of the angioma was not detected until his readmission to the hospital for study on March 1, 1928, over five years after the cerebellar operation.

During this interval vision in the left eye had become impaired, and the house officer, Dr. Fulton, aware of our interest in Lindau's disease, quickly recognized that the large, tortuous vein previously noted was accompanied by what was an abnormal artery, the two passing out of vision, with the pupil undilated, in the lower periphery of the retina. In addition, the retina showed an extensive proliferative retinitis which certainly had not been present three years before, for it could hardly have escaped notice. The fields of vision taken before the operation in 1922 had shown no defects, but

at this time there was a marked distortion in the affected eye (Fig. 3).*

Dr. George S. Derby kindly saw the patient for us at this juncture and dictated the following note. Certain of his statements that seemed to us of special interest we have taken the liberty of italicizing.

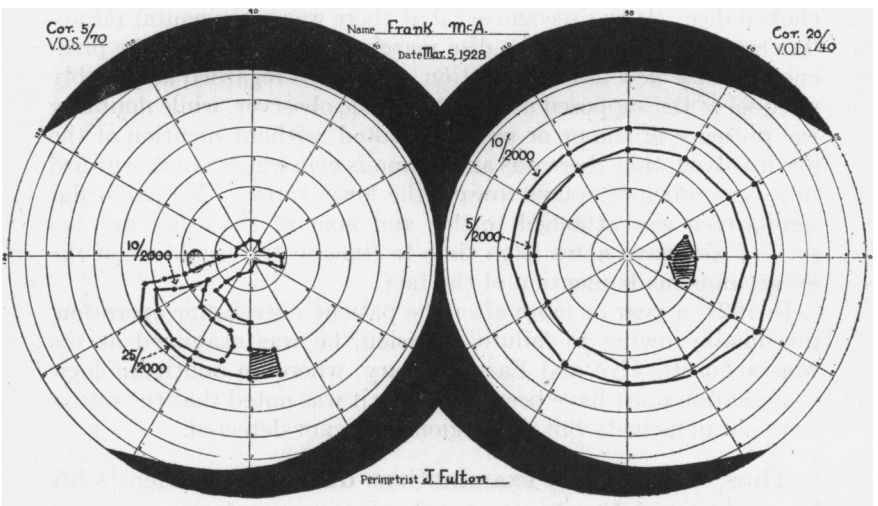


Fig. 3.—The fields of vision (screen) five years after patient's operation in 1922.

L. E.: Posterior adhesion [iridocyclitis] of the iris to the lens at 6 o'clock. A dot on the posterior surface of the lens slightly on the nasal side. Except in the upper temporal quadrant, the disc is blurred in outline, owing to astigmatism, and below the outline cannot be distinguished. The vessels come out of the lower central part of the disc. The superior nasal artery is extremely small and divides into three branches which run upward. Two veins run upward also, one to the nasal side and one slightly upward toward the temporal side. There is a patch of pigment on the temporal margin of the disc; and off the edge of this, almost connecting with it, is a large, irregular, whitish patch (probably formation of

* Fields plotted two months later, on May 16, 1927, show still further constriction, so that the process is doubtless rapidly advancing to blindness.

fibrous tissue in the deeper retinal layers) with considerable pigmentation on the margin toward the nerve.

The temporal margin of this patch is irregular and sends two processes far out toward the periphery of the fundus. The vessels in this region seem to be in reasonably good condition. These patches show areas of pigmentation. The patch extends downward on the temporal side of the macular region and reaches down below it.

On the nasal side of the disc there is a similar fibrous patch which shows some pigment and marked irregularity of the edges extending out to the periphery as far as can be seen. These patches are underneath the retinal blood-vessels.

The lower blurred margin of the disc shows two relatively enormous vessels. An *artery on the nasal side, which is four or five times the normal size,* passes through a rather edematous area, and at about one disc-diameter below the disc its caliber narrows to the size of a normal artery. It then dilates again almost to its original size, and runs downward and outward temporally until it crosses the vein, perhaps three or four disc-diameters below the nerve. *This artery shows a very characteristic beading in different portions of its course.*

The second vessel on the temporal side is a *vein of enormous caliber,* which looks nearly twice as large as the artery and is quite tortuous in its course. This runs downward and slightly outward to the place where it passes under the artery. At this point it is possible to see that the artery makes a slight indentation on the vein. As the vessels lie alongside of each other, *it is difficult to tell from their color which is artery and which is vein.*

At the point where these vessels cross there is a pear-shaped patch of atrophy where the sclera shows through. There is a slight pigmentation on its nasal margin. The lower part of the retina shows a tigroid pigmentation. The artery, after crossing the vein, gradually becomes somewhat smaller and runs downward and temporally. The vein also runs downward in a parallel direction to the periphery and, at the limit at which one can see, *both vessels disappear in a prominent rounded nodule* which can best be seen with a +12 sph. It has some white fibrous tissue on its superior margin, but elsewhere has a pink color. The surface is covered with a number of small blood-vessels. The mass appears fairly sharply localized. One cannot see how far forward it extends, but from side to side it certainly is not over a disc-diameter at this

point. The upper border is hemispheric and it definitely protrudes from the underlying retina at least 2 or 3 D.*

There is an occasional cholesterin crystal seen in the central area, and on the nasal side also. Beautiful cholesterin crystals are seen above and in the macular region.

The disc is oval and within normal limits. *It is so badly outlined below that it almost looks like choking.* I can see no pulsation. The artery passing above it is undoubtedly small. The whole superior nasal artery which divides near the disc is very small and shows perivascular changes along most of its length, whereas the superior temporal artery is of normal size.

R. E.: Here the iris dilates normally; media are clear; nerve-head is rather small, with slight indentation on the nasal side above and below and rather pale on the temporal side, with a shallow physiologic cup. Cilioretinal vessel at 8 o'clock; a faint choroidal ring on the temporal side of the nerve. The arteries in this eye are extremely small throughout. These have a silver wire reflex and a perivascular sheath runs along them for some distance from the disc, which is very marked on the lower temporal branch. Where they cross the veins there is a slight imprint made. The veins also seem to be perhaps a bit smaller than normal. Tigroid fundus.

Both the right and left eyes are best seen with a +9 sph.

A hemangioblastoma of the nervous system is a relatively benign lesion. It is important, therefore, that an ophthalmologist who finds one of these lesions in the retina should realize the need of looking for cerebellar symptoms, since a cerebellar tumor of like sort most favorable for operation may be coexistent. It is obviously no less important that a neurosurgeon, desiring to make, so far as possible, an exact pathologic diagnosis of a cerebellar lesion before operation, should know of the existence of retinal angiomas and something of their appearance.

As *angiomatosis retinæ* was a condition quite unknown to us, we have been through the literature of the subject and venture to give a brief historic statement concerning it,

* In the color sketch of the fundus kindly made for us under Dr. Wilmer's direction the lesion had been brought more fully into view by the aid of prisms.

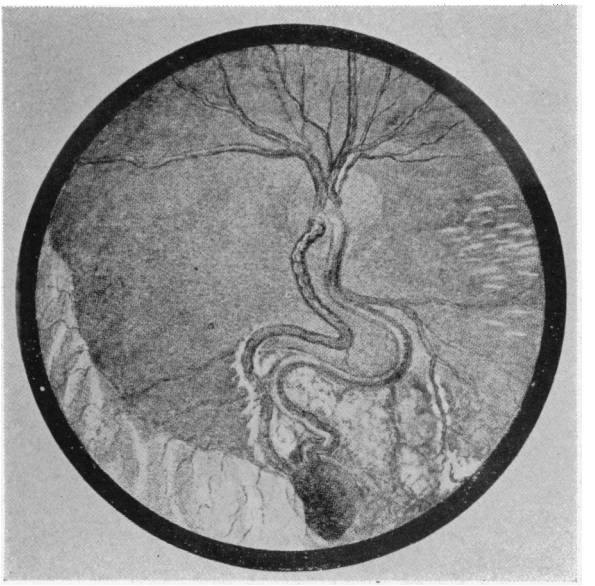


Fig. 4.—Case of Scarlett. Note the angiomatous nodule in the lower part of the field, the beaded artery, the enlarged vein, exudation, and detachment of retina.

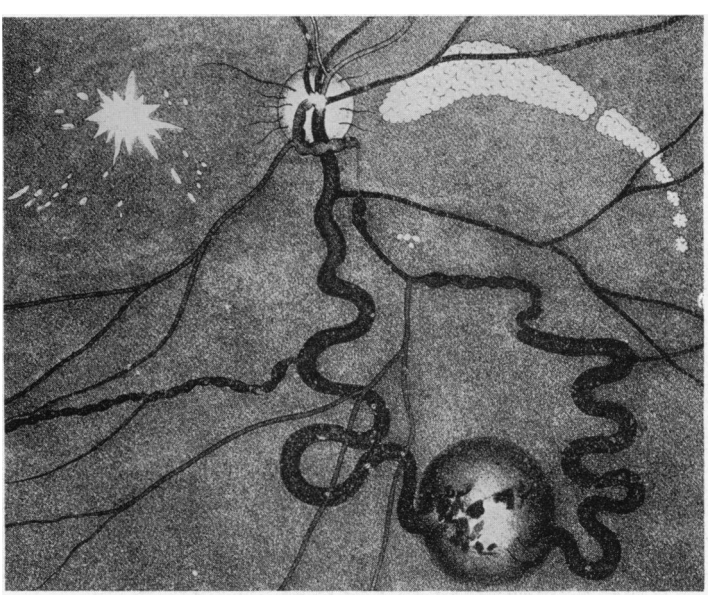


Fig. 5.—The earliest illustration of a case of retinal hemangioma described as an arteriovenous aneurysm (Fuchs, 1882). Note the beaded artery to the right.

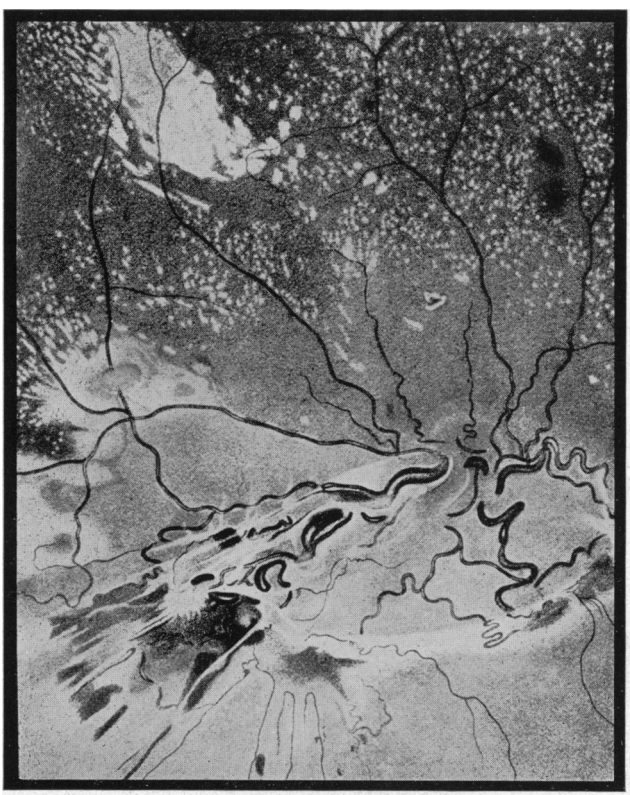


Fig. 6.—Wood's case (1892) of "retinal detachment with unusual dilatation of retinal vessels." Eye enucleated subsequently and examined by Treacher Collins (1894), who described the underlying lesion as a capillary nævus.

accompanied by a few illustrations of some of the better known examples* for the benefit of others who may be, as we were, similarly uninformed. So far as we are aware, the only case described in this country was reported in 1925 by Scarlett[34] (Fig. 4), who gives a typical illustration of the lesion after it has begun to cause secondary changes in the retina.

The first unmistakable example in the literature was clinically recorded in 1882 by Fuchs,[14] who interpreted the ophthalmoscopic picture (Fig. 5) as an arteriovenous aneurysm. It is possible that even before Fuchs a far-advanced case may have been observed and one eye studied anatomically by Panas and Rémy (1879),[31] the other eye of the same patient having been later described clinically by Darier (1890)[10] as a sort of retinitis proliferans. The true nature of the disease, however, was first recognized by Treacher Collins (1894)[7] who examined the eye of a patient with an advanced retinal lesion that had been briefly described and pictured (Fig. 6) the year before by Wood (1892).[38] Collins not only called attention to the familial character of the disease, for the sister of the patient was similarly afflicted, but concluded, after a careful microscopic study, that the essential lesion was a "capillary nævus which in places had undergone cystic degeneration."

In the years following an ophthalmoscopic description of other cases was given: by Goldzieher (1899),[17] who was obscure in his explanation of the pathology of the lesion; by von Dzialowski (1900),[13] who spoke of it as an "Aneurysmenbildung," and by Leplat (1901),[26] who likewise ascribed the appearance to a congenital arteriovenous aneurysm.

In 1904 v. Hippel[21] reported his two cases, the first of which (the patient, Otto Meyer) had been shown at the Heidelberg Congress in 1895 as having "an unusual disease of the retina"

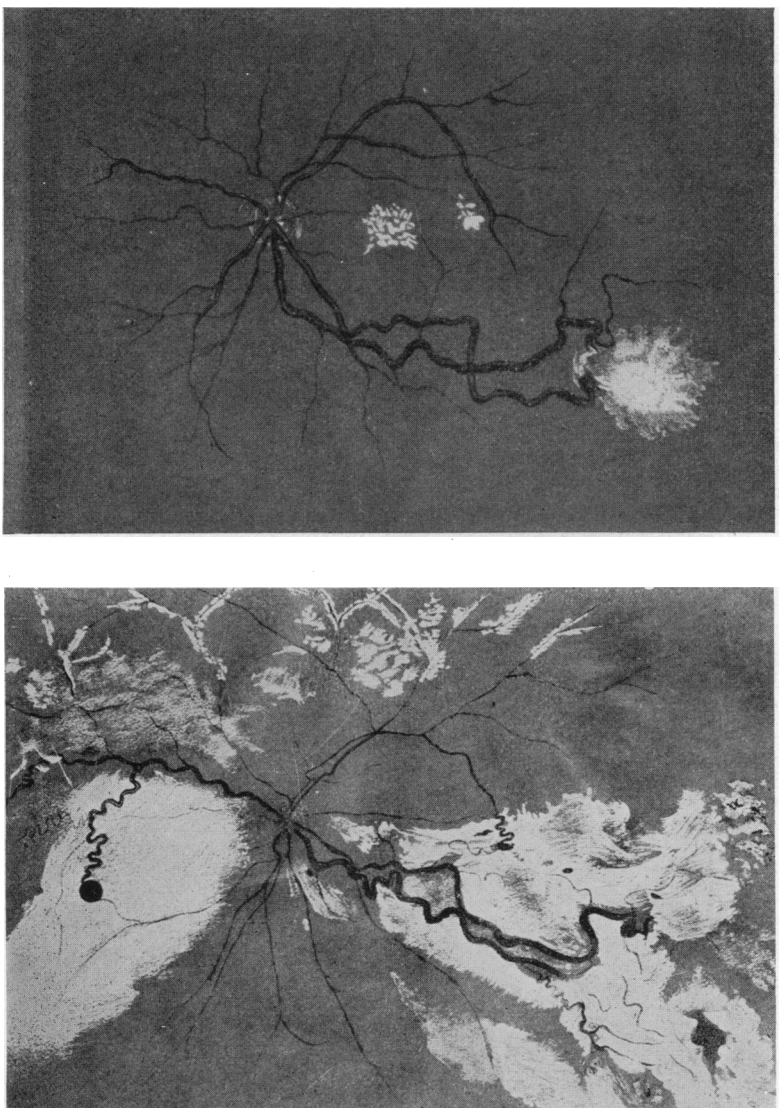
* An excellent review of the subject to 1916 will be found in Prof. Th Leber's article in the *Graefe-Saemisch-Hess Handbuch der Gesamten Augenheilkunde*, II Teil, Bd. vii, p. 1966–1994.

without other explanation than that it might be retinal tuberculosis. This notable article was accompanied by a series of four excellent illustrations in color of the eye of Otto Meyer, which show the advance of the process between the year 1893 (Fig. 7), when the lesion was first observed, and 1896 (Fig. 8), by which time multiple foci had become apparent. The single illustration (Fig. 9) of the eye of von Hippel's second patient (Otto Möbius) shows the condition to have been approximately in the same stage as that in our own patient.

It was not until seven years later that von Hippel had an opportunity to gain, in one of these cases (Otto Meyer's), first-hand knowledge of the pathology of the lesion. Meanwhile Czermak (1905),[9] just before his untimely death, had made a brief report of the microscopic study of the eyes of Goldzieher's patient, the lesion, in spite of its advanced stage (Fig. 10), having been shown to be a true capillary hemangioma.

Shortly after this Coats in England published (1908)[5] his remarkable paper on exudative retinal disease, the last section of which is given over to a discussion of the later stages of the cases in question in which there was assumed to be an arteriovenous communication. That Coats was thought by others to have had the malady in question under consideration is shown by the fact that soon after (1910) another case, accompanied by an illustration in color of an unmistakable angioblastoma of the retina (Fig. 11), was reported in England by Pooley,[32] who merely refers his readers to Coats' admirable description of advanced stages of the condition.

In 1911 appeared v. Hippel's second paper,[22] containing an account of his own studies of one eye of the patient, Otto Meyer; and having meanwhile learned of the earlier findings of Treacher Collins, of Czermak, and of Coats, with which his own agreed, he chose, doubtless because of the multiple hemangiomas that were present (*cf.* Fig. 8), to designate the



Figs. 7 and 8.—V. Hippel's Case 1 (Otto Meyer), showing advance of lesion from November, 1893, to March, 1896.

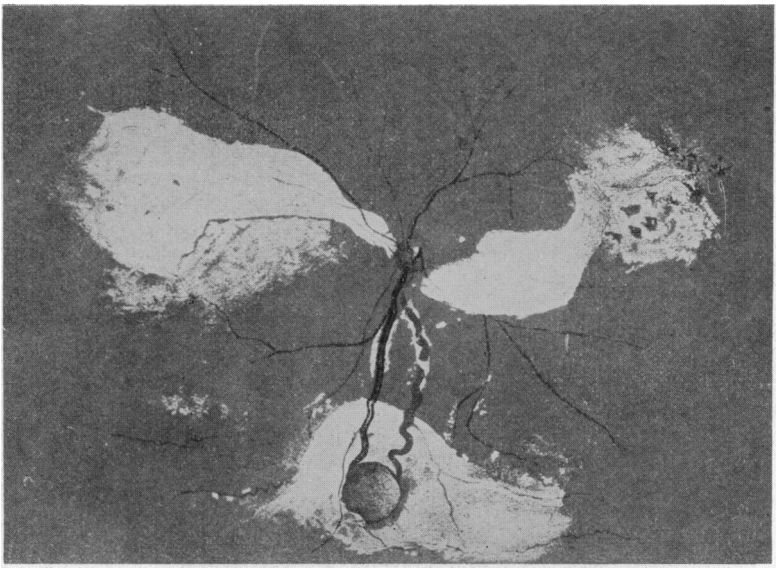


Fig. 9.—V. Hippel's second case (Otto Möbius), showing typical "six o'clock" angioma with somewhat advanced retinal change.

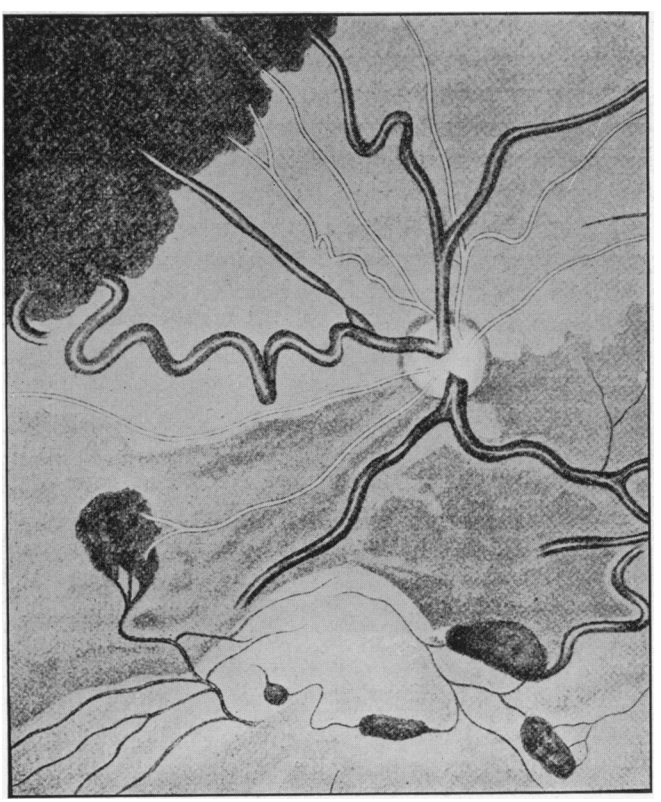


Fig. 10.—The Goldzieher (1899)-Czermak (1905) case. The first case after Collins correctly diagnosed as a capillary hemangioma in spite of the highly advanced exudative process that led to the enucleation.

condition *angiomatosis retinæ*. Shortly after this, in 1912, came Coats's second paper on *retinitis exudativa*, a perusal of which leaves one somewhat more confused about the conditions he is describing than did the last section of his first paper.

Between the years 1911 and 1921, though many clinical cases were reported [*e. g.*, those of Moore[30] (Figs. 12 and 13) and of Ditróí [11, 12] (Figs. 14 and 15)], confusion regarding the exact pathologic nature of these angiomatous lesions was caused by the papers of Meller (1913),[29] of Ginsburg and Spiro (1914),[16] and of Guzmann (1915),[18] all of whom reported typical examples of the disorder, but regarded the process, owing to the secondary changes which occur, as a gliosis or angiogliomatosis of the retina (*gliosis retinæ diffusa telangiectoides*). The confusion, in other words, was the same as that which has reigned in regard to the histopathologic nature of the hemangiomas found in other parts of the nervous system, the excessive vascularity being regarded as a reactive rather than a primary incident in a gliotic process.

Meanwhile, however, Leber's excellent review of the subject had been published (1916),[25] the lesion in an early case (Fig. 15) had been subjected to study by Gamper (1918),[15] and finally the papers by Brandt (1921)[4] and by Berblinger (1922)[3] served definitely to establish the true pathology of the primary lesion. In one of Brandt's three cases the eye had been removed sufficiently early to have been unaccompanied by the secondary exudative changes and gliosis that so often confuse the histologic picture. The lesion happened to be a cellular rather than a capillary type of hemangioma which he termed an "endothelioma," but his pictures show it to be a typical hemangioblastoma. Brandt correctly emphasized that the lesion was a true tumor and differed from the congenital angiomas in other parts of the body in that it did not begin to show clinical evidence of its presence until the third decade, on the average.

Up to this point attention has been paid to the retinal lesions alone, but the story by no means ends here. In 1912 Seidel,[35] in a report before the Ophthalmological Society in Heidelberg of a typical case (Fig. 17) in an early stage, called attention to a fact previously unemphasized, namely, that a cerebellar cyst had been found at autopsy in Czermak's patient, whereas his own patient, curiously enough, had developed a choked disc with cerebellar symptoms and a cyst had been demonstrated by puncture. What is more, it was known that the patient's brother had died after an operation for a cerebellar cyst. He pointed out, too, that v. Dzialowski's (1900)[13] patient had a choked disc and that a post-neuritic atrophy was recorded in Jakoby's (1905)[23] case.

Nearly ten years passed before this interesting observation appears to have been in any way supplemented. In the article by Brandt (1921),[4] to which we have referred, is described the necropsy on v. Hippel's original case (Otto Meyer), who, seventeen years after being first reported, had died of intracranial symptoms. There was found, in addition to a tumor of the right retina (the left eye had been previously enucleated), tumors of the tip of the right petrous bone, the convexity of the left cerebellar hemisphere, and of the cauda equina. These were taken to be metastatic from the eye, but when examined microscopically, appeared to be metastases from a malignant hypernephroma, although no primary hypernephroma was found in the region of the kidneys.* He decided finally that the tumors were probably neither metastases from the retinal tumor nor from a hypernephroma, but that there was a simultaneous primary formation of numerous tumor nodules and that there was no necessary connection between the retinal tumors and the others.

A year later Berblinger (1922)[3] described another case (Fig. 18) in which an angioma of the retina was associated

* The close resemblance of the cells of certain of these hemangioblastomas to those of a hypernephroma has been pointed out by Lindau.

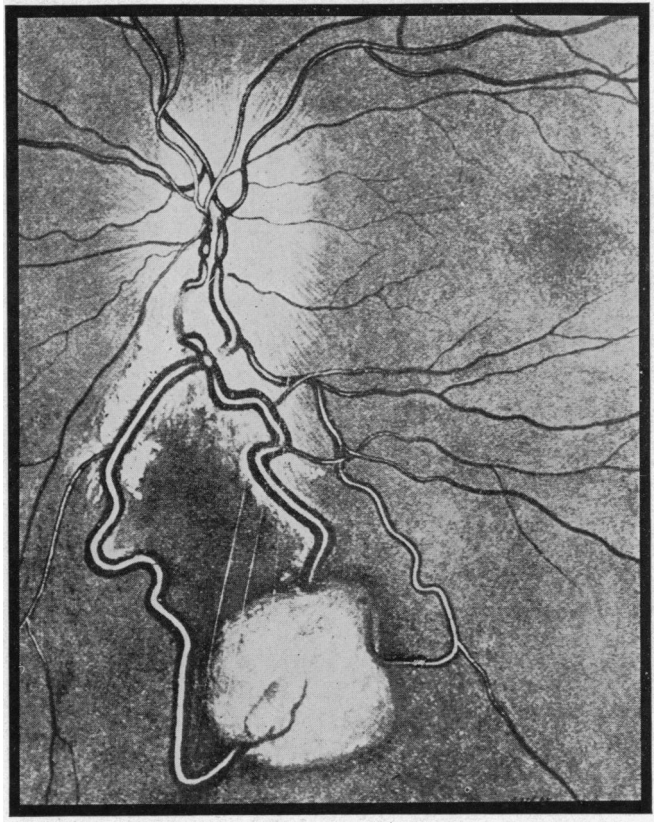
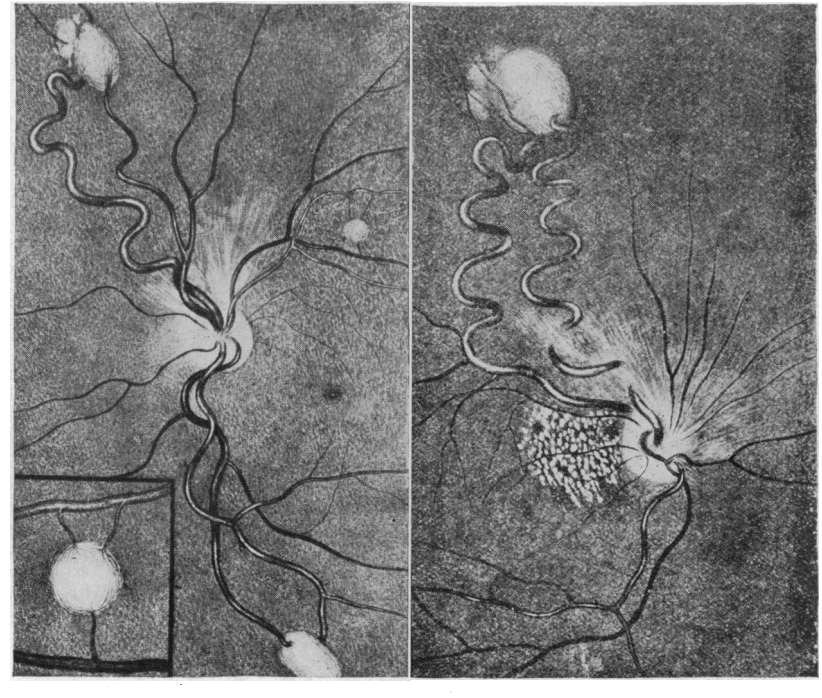
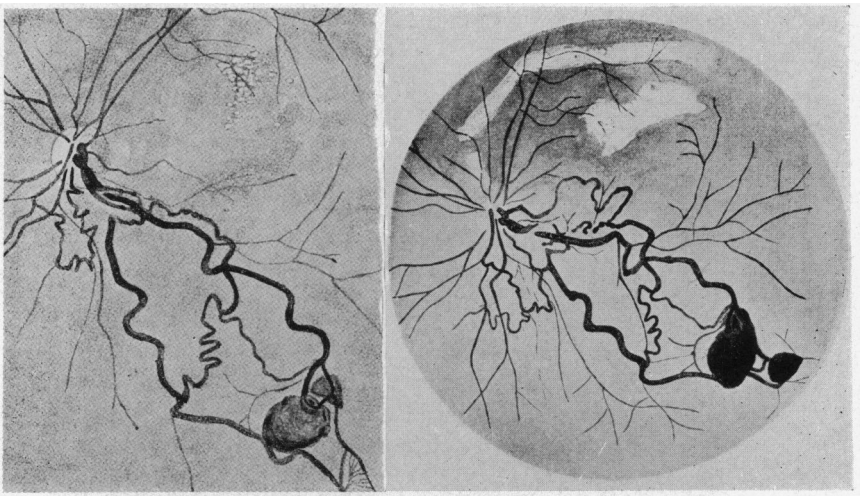


Fig. 11.—Pooley's case of "retinal angioma." Note beaded condition of artery.



Figs. 12 and 13.—Moore's case (1912) with bilateral angioma: Left eye with multiple lesions; right eye with single lesion.



Figs. 14 and 15.—Ditrói's case, showing slow advance in process between 1914 and 1919. Note increased vascularity with beaded condition of artery; fusion of former two nodules with an additional one appearing; increasing retinitis.

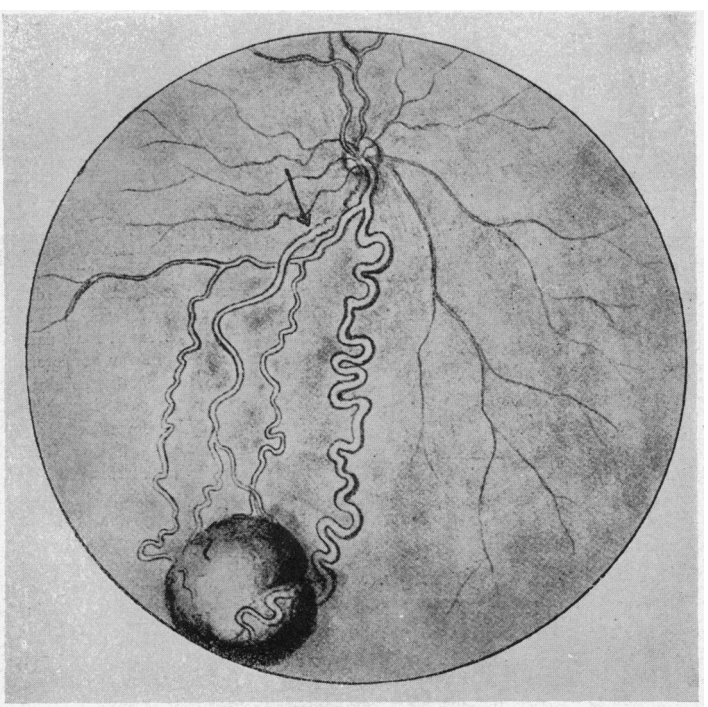


Fig. 16.—Gamper's case, 1918. Eye removed because of blindness with severe headaches (possibly cerebellar). Note hint of beaded condition of artery (arrow); lesion described as a telangiectasis.

with multiple tumors elsewhere in the nervous system, one of them in the lower half of the medulla oblongata having been shown microscopically to be a typical capillary hemangioma. Heine (1923),[20] who examined the eye of Berblinger's patient, did not escape from the confusion of many of his predecessors and concluded, after a careful study, that the tumor of the retina was an "angiogliosis"; he expressed himself as being more inclined to regard the case as an example of Coats's retinitis exudativa than of v. Hippel's disease. Berblinger, however, properly insisted that Heine's term, angiogliosis, fails to emphasize the essential character of the primary retinal lesion which he takes to be a hemangioma, and of which the exudation and the gliosis are but a secondary irritative reaction; he believed that the tumors found in the eye and in the medulla were independent of each other, and resulted from a dysontogenetic blastomatous growth.

Five years later (1926) appeared Lindau's illuminating paper,[27] in which all these obscurely associated observations were brought together and their true relationship clearly shown. He pointed out that in the examination of v. Hippel's original case Brandt (1921) had found, in addition to the lesions in the central nervous system which we have mentioned, cystic kidneys, cystic pancreas, and tumors of the epididymis, spleen, and cartilages. He called attention to the fact that Koch, in 1924,[24] in describing a cystic pancreas, noted that there were present in the same individual cystic kidneys, cavernoma of the liver, and hemangiomas of the spinal cord and the cerebellum; also that in the Berblinger-Heine case a cystic pancreas was found.

Many other such cases, among which we may mention that of Bassoe and Apfelbach (1925)[2] as having been published in this country,* have also been picked up by Lindau from the

* The medullary tumor was described by these authors as a glioma but has been shown by subsequent examination to be a typical capillary hemangioma.

literature and doubtless many more will follow now that attention has been drawn to the matter. And, as was mentioned at the outset, three cases have been reported during this past year (1927) by Rochat,[33] by Wohlwill[37] and by Shubaack,[36] the last having for the first time used the eponym, Lindau's disease.*

And so, as stated in the introductory paragraph, a variety of associated lesions, notable among which are cerebellar and retinal hemangioblastomas, have been assembled by Lindau in a pathologic complex and placed upon a basis of maldevelopment of the mesoderm in the third fetal month.

CONCLUSIONS

The typical picture of angiomatosis retinæ of v. Hippel consists of a pair of hugely enlarged vessels, often emerging from the lower part of the disc to disappear in a small tumor mass in the peripheral retina. The vessels, though of approximately the same color, can be distinguished by the fact that the vein is the larger of the two, whereas the artery is often beaded and of varying caliber. Not infrequently, in course of time, other small tumors may appear in other parts of the retina with the development of a similar pair of vessels.

The process slowly advances, with the ultimate occurrence of secondary changes in the shape of opacities and infiltrations due to exudative secretion and sometimes to hemorrhages, with the formation of a reactive gliosis, iridocyclitis, detachment of the retina, glaucoma, and so on, which may necessitate enucleation. These secondary changes, which fall in the category of Coats's proliferative retinitis, ultimately

* Of these three recent reports, that by Rochat is particularly noteworthy. It concerns a family in which in the first generation the mother died of an unknown lesion of the brain. In the second generation, of five children three brothers were affected, one with angiomatosis retinæ and another with cerebellar tumor. The third brother had an angioma of the right retina and died following an operation for cerebellar tumor. A necropsy was obtained, but no mention is made of the condition of the abdominal organs. In the third generation, one boy has developed angiomatosis in both retinæ.

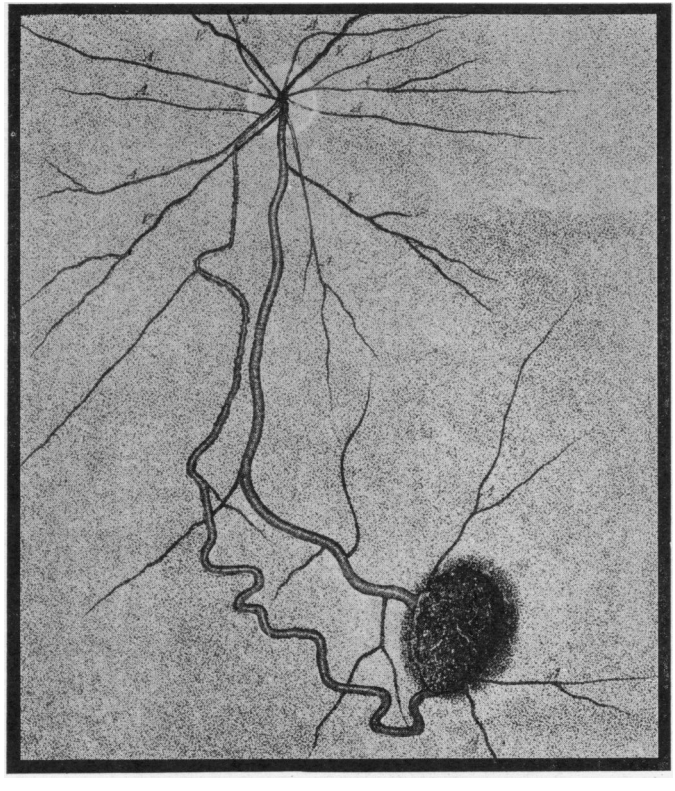


Fig. 17.—Seidel's typical case (1912), which was familial and in which cerebellar symptoms were recognized. Note beaded artery.

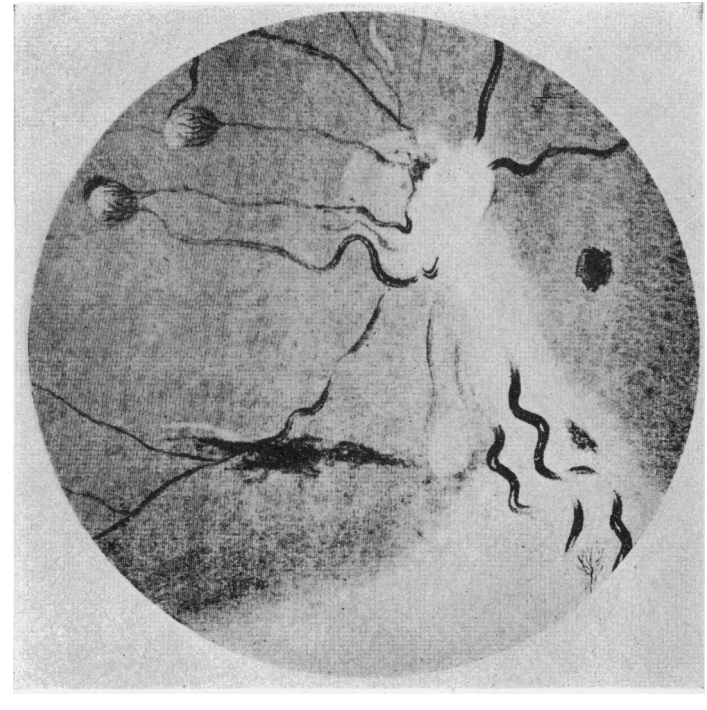


Fig. 18.—Berblinger's case, described by Heine (1923) as an inflammatory intra-ocular pseudotumor with retinal cysts; subsequently shown by Berblinger to be due to a capillary hemangioma.

serve to conceal the nature of the primary lesion. Both eyes are likely in time to become involved, and the condition has been found in many cases to be familial.

Though the histologic nature of the underlying lesion remained for a long time obscure, it is now known to be a hemangioblastoma, a form of tumor which exudes plasma and tends to produce cysts having xanthochromic fluid contents. It, moreover, has come to be appreciated that coincidental hemangioblastic cysts are not infrequently found in the cerebellum arising usually from an anlage over the posterior part of the fourth ventricle.

Lindau's studies have served to show that these angioblastic lesions of the nervous system are not infrequently found in association with cysts of the kidney, cystic pancreas, hypernephromas, and tumors of the adrenal glands.

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DISCUSSION

DR. GEORGE S. DERBY, Boston: Dr. Cushing was kind enough to let me see this case and study it. This is a subject of much interest, and I feel that Dr. Cushing has done us a great service in coming here and calling our attention to the very wide ramifications of this disease, so that when next we see a case of von Hippel's disease, or the appearance that von Hippel described, we will know it, as well as some of the conditions which Coats has described. We must remember that we may have changes in other parts of the body which we should look for.

Dr. Wilmer's illustration is certainly very beautiful. If I were to make any suggestion regarding it I would say, as Dr. Cushing did, that it seems to me that the color of the artery and vein very nearly approach each other, and it would be extremely difficult to tell one from the other. Also that perhaps the beading of the artery was a little more marked than shown in Dr. Wilmer's very beautiful drawing.

DR. W. H. WILMER, Baltimore: It was extremely difficult to make a satisfactory reproduction of the very interesting case which Dr. Cushing has so delightfully presented to this Society.

The patient was available for only one day. He had a hyperopia of over 7 D., there was a lenticular opacity, and, at 6 o'clock, a posterior synechia. Care was exercised to reproduce the fundus changes as faithfully as possible. The eyeground was studied with the Gullstrand ophthalmoscope and the red free light, as well as with the ordinary ophthalmoscope. In addition, the fundus changes were examined by a number of persons and the color

values of the different fundus conditions discussed. It would be possible to improve upon this illustration if the patient were available for comparison with the drawing, and if Dr. Cushing could send at the same time notes and suggestions upon the case.

The tumor proper was below and so far out in the periphery of the retina that it was very difficult to see, but a 12° prism held before the patient's eye by an assistant was helpful.

In addition to the hyperopia, synechia, and cataract, the afflicted eye was the left one, which added somewhat to the artist's difficulty in getting a faithful representation of the condition.

DR. EDWARD JACKSON, Denver: I would suggest that if Dr. Cushing, or Dr. Wilmer, or any one who has such a case, could loan it to Dr. Bedell for a few moments, a record could be made that would be of great scientific value.

DR. ALLEN GREENWOOD, Boston: I think this case is helpful in one particular—that it should make us more careful in examining the periphery of the retina in obscure cases. I saw this man when he was seven and he had 9 D. of hyperopia under a cycloplegic. With no glass could I improve the vision above 20/70 in each eye. I saw him only once, but I did get a history that the father had poor vision. I have no record of finding anything abnormal in the fundus.

DR. LUCIEN HOWE, Belmont, Mass.: I rise to express my appreciation of what has been presented here, and also to call attention to a point which Dr. Cushing mentioned, and which I think this Society should appreciate, the importance of the hereditary tendency of this condition. I think we must consider that.

DR. HARVEY CUSHING, closing: In answer to Dr. Greenwood's question, I may say that Lindau has written another paper on the subject this past year. His first paper appeared in 1896, and the second paper was given before the German Ophthalmological Congress. In it he reports four additional cases, all of which had come to a postmortem examination. One of them was personally observed by Lindau—a typical angiomatous cyst of the cerebellum having been found. Lindau felt sure that there must be an angioma of the retina, and although the eyegrounds appeared to be normal, serial sections were made and a microscopic hemangioma actually was found.

It may be that in the children of our patient there are latent angiomas of microscopic size that, from trauma or something else, may some day become active. Not until that time comes will the vessels begin to enlarge. I doubt whether the patient had anything observable in his eyegrounds in childhood.

I am asked whether there was any difference between the present appearances of the eye and that seen in 1922. The difference is great. Our attention would certainly have been attracted to the present condition of the retina even had the dilated vessels not escaped interpretation. He did not have the iridocyclitis at 6 o'clock that Dr. Wilmer speaks of. We could hardly have failed to observe such a gross change.

THE VALUE OF MOVING PICTURES IN OPHTHALMOLOGIC TEACHING

A PRELIMINARY REPORT

C. E. G. SHANNON, M.D.
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AND
W. J. HARRISON, M.D.
Philadelphia
(By invitation)

Like other inventions that were at first regarded only as interesting but ultimately became of value in modern life, so the moving pictures, in their earlier stages more or less amusing and spectacular, have gradually proved of practical merit in the fields of industry and the arts. They have now definitely entered the field of medicine, and are proving to be of worth in our teaching departments. Isolated and fragmentary films on matters of medical interest have been made from time to time in the past, but now it seems that the successful future of the medical film lies closely parallel to the printed literature of medicine, for, after all, the film is a potential form of literature. In time it will acquire form and style, just as has paper literature.